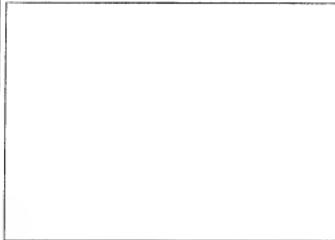


In The United States Patent Office

5



Serial No. : 10/516,500
Filing Date: 29 November 2004
Group Art: 1625
Examiner: Niloofar RAHMANI, Esq.

SUPPLEMENTAL RULE 132 DECLARATION

20

I am an inventor of record of the captioned application. I present this
Supplemental Declaration pursuant to The Code of Federal Regulations, Title 37,
Rule 132. I hereby Declare as follows:

1. The Examiner's 1 August 2006 Office Action presents a chemical diagram

of a chemical structure which

the Examiner asserts has a

CAS Registry Number 5508-

5 58-7. The chemical diagram

provided in the Office Action

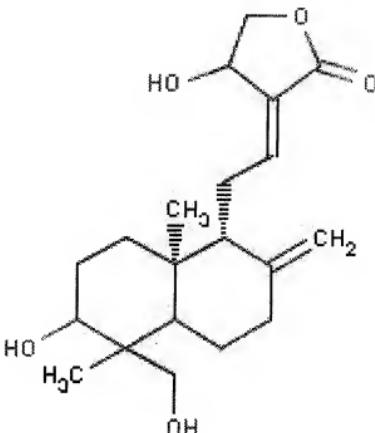
is not, however, clearly legible.

I accordingly show here the

chemical structure diagram of

10 the chemical compound with

CAS Registry Number 5508-



15 58-7. This structure was obtained from the National Library of Medicine's

Specialized Information Services web site. I enclose a print out of the web

page containing this information. Moieties illustrated in red have specific

stereochemical configurations. Contrary to the poorly-legible structure

shown in the Office Action, the National Library of Medicine's Specialized

Information Services compound with CAS Registry Number 5508-58-7 has

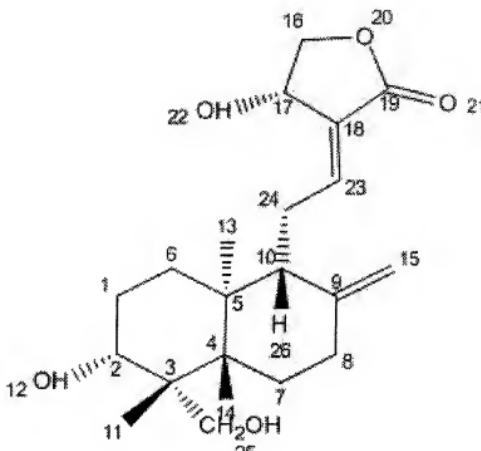
no sulfur atoms nor any "R-" substitutable moieties.

2. In contrast to the compound of CAS Registry Number 5508-58-7, our claims are drawn to a compound with the IUPAC designation, "3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone." I illustrate the structure of it

5

10

15



here. For the convenience of the Board of Patent Appeals and Interferences, I provide on this structure reference numbers for the atoms.

3. I infer that the Examiner intends to allege that the compound with CAS Registry Number 5508-58-7 is the same as the claimed compound. I respectfully disagree. Rather, the structural differences between the Examiner's compound and the claimed compound are readily apparent when one compares the two chemical structures. For example, the claimed

5 compound bears a methyl group at #14; in contrast, this group is completely absent from the compound of CAS Registry Number 5508-58-7. Similarly, the stereochemical configuration of the claimed compound, at, *e.g.*, atom numbers #10, 11 19, 20, 26 (and perhaps #12, 17, 19, 20 and / or 25 as well), is different from the stereochemical configuration of the compound of CAS Registry Number 5508-58-7. One of skill in the art would, on seeing these two different structures, immediately apprehend that the compounds are not the same, and may indeed possess different pharmaceutical and toxicology profiles.

10 4. The National Library of Medicine entry for the compound of CAS Registry Number 5508-58-7 confirms my assertion in my previous Declaration that the meaning of the term “Andrographolide” is neither well-known in the art nor denotes one specific compound. The compound shown in the National Library of Medicine is different from the compounds shown in the Examiner’s own references (*e.g.*, U.S. Patent No. 5,883,074; US Patent Application 15 2002/0077350 and US 2002/0068098). Each of these sources, however, refers to their diverse compounds as “andrographolide.”

I further hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both,
5 under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

10 Professor Juan Luis HANCKE OROZCO, Ph.D.
Dated as of 20 September 2006



15

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FORM

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Total Number of Pages In This Submission

Application Number	10/516,500
Filing Date	29 Nov 04
First Named Inventor	H.L. HANCKE
Group Art Unit	1625
Examiner Name	N. RAHMANI
Attorney Docket Number	HPInارد.

ENCLOSURES (check all that apply)

<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Assignment Papers (for an Application)	<input type="checkbox"/> After Allowance Communication to Group
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment / Reply	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)
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<input checked="" type="checkbox"/> Affidavit(s)/Declaration(s)	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Request for Refund	
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Response to Missing Parts/ Incomplete Application		
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Mark Pohl, Esq., USPTO Reg. No. 35,325 Pharmaceutical Patent Attorneys, LLC 55 Madison Avenue, 4th floor, Morristown, NJ 07960-7397 USA
Signature	/s/
Date	see below date

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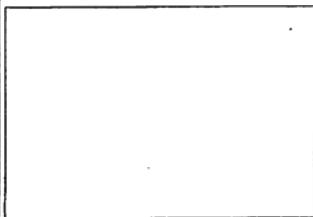
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In The United States Patent Office

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Serial No.: 10/516,500
Filing Date: 29 November 2004
Group Art: 1625
Examiner: Nilofar RAHMANI, Esq.

RULE 132 DECLARATION

20

I am an inventor of record of the captioned application. I present this Declaration pursuant to The Code of Federal Regulations, Title 37, Rule 132. I hereby Declare as follows:

25

1. I have read the Examiner's 1 August 2006 Office Action and the references cited therein. I respectfully disagree with certain of the factual allegations made by the Examiner because the art of record contradicts the Examiner.
2. The Examiner alleges, "*Andrographis paniculata* grown just anywhere everywhere on this planet may or my [sic] not have the compounds necessary to treat Syndrome X." I respectfully disagree, for several reasons.

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Diterpenic Lactones . . .

3. First, *Andrographis paniculata* cannot, to my knowledge, grow "anywhere everywhere on this planet." To the contrary, like any other plant, it has specific environmental conditions for growth; these conditions are well known in the art, and well known to any botanist familiar with the plant.

5 4. Second, I have no reason to believe that "*Andrographis paniculata* . . . may or my [sic] not have the compounds necessary to treat Syndrome X." To the contrary, every specimen of *Andrographis paniculata* which I have evaluated, from whatever source or ecosystem, has in fact contained "the compounds necessary to treat Syndrome X." I therefore know of no factual evidence to support the thesis that *Andrographis paniculata* from a certain 10 specific ecosystem "may or my [sic] not have the compounds necessary to treat Syndrome X."

15 5. Our application claim number 53 reads as follows:

53. A method comprising:

i. diagnosing in a patient a disease selected from the group consisting of: Alzheimer's Disease; Acquired Immune Deficiency Syndrome; and autoimmune disease, and

20 ii. administering to said patient 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone in an amount effective to combat said disease.

I understand that "It is the examiner's position that the claims are drawn to 'a method of diagnosing in a patient a disease.'" I respectfully disagree because the

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Examiner's position ignores the entire second half of our claim. Contrary to the Examiner's position, one of skill in the art would read this two-step claim to be drawn not to a one-step method (diagnosing), but to a two-step method requiring both i) diagnosing and ii) administering.

5 6. I understand the Examiner to allege that the meaning of the term "Andrographolide" is well-known in the art and denotes one specific compound. I respectfully disagree. The Examiner's own references show that this term is used by different scientists to denote different compounds. For example, the Examiner notes that U.S. Patent No. 5,883,074 uses the term to denote one compound, while US Patent Application 2002/0077350 and US 10 2002/0068098 use the same term to denote a different compound.

10 7. I understand the Examiner to allege that the compound allegedly known as "andrographolide" is the same as the claimed compound. As support, the Examiner at page 3 of her Office Action illustrates the compound which she understands to be the same as the claimed compound. I respectfully disagree that the Examiner's compound is the same as – nor even similar to – the claimed compound. Rather, the structural differences between the Examiner's compound and the claimed compound are readily apparent when one compares the two chemical structures. I illustrate the differences here,

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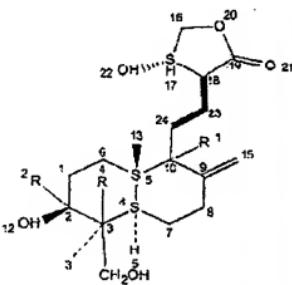
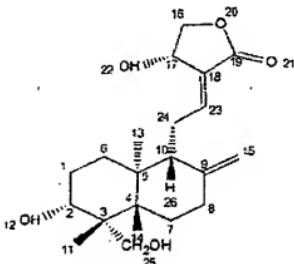
Priority Date: 03 February 2004

Diterpenic Labdanes . . .

showing the structure of the claimed compound on the top, and the structure of the Examiner's compound on the bottom. One of skill in the art would, on seeing these two different structures, immediately apprehend that the compounds are not the same, and may indeed possess widely different pharmaceutical and toxicology profiles.

5 8. As a related matter, the Examiner at pages 3-4 provides the incorrect IUPAC nomenclature designation for her compound. While a precise IUPAC designation is not possible (the Examiner's compound bears a number 10 of substituted R moieties), the Examiner's compound includes three sulfur atoms. The IUPAC name she provides, however, makes no mention of any of these.

15 The Examiner's compound



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9. I further note that the art of record fails to teach the claimed compound. The prior art teaches "andrographolide." See e.g., BABISH *et al.*, U.S. '098. Our claims, however, do not require "andrographolide"; rather, our claims require 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone. This compound is not taught by the art of record. This is illustrated in the accompanying comparison of the claimed compound and the five compounds taught by the art of record.

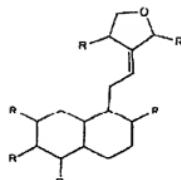
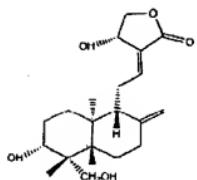
DECLARATION - Page 5

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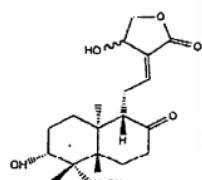
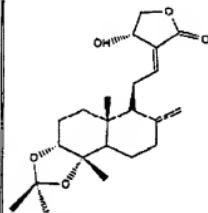
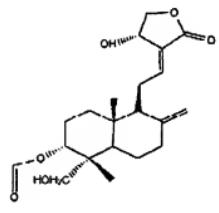
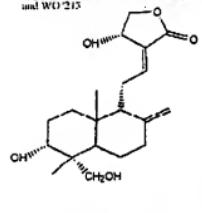
Serial No. 10/516,500

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John G. BABISH *et al.*, WO '605

The claimed compound

John G. BABISH *et al.*, U.S. '994, G.D. WHEELOCK *et al.*, U.S. '063 and WO '213NANDURI *et al.*, U.S. '324NANDURI *et al.*, U.S. '196NANDURI *et al.*, U.S. '590

For example, BABISH *et al.*, WO '605 and NANDURI *et al.*, U.S. '324, U.S. '590, and U.S. '196 (2002) fail to teach methylation at C4. Similarly, BABISH *et al.* U.S. '098, and WHEELOCK *et al.*, U.S. '994, U.S. '063 and WO '213 fail to teach oxidation at C9. One of skill in the art would not read any of the references of record to teach nor fairly suggest the claimed compound.

5

10. Similarly, our claims are drawn to methods to treat AIDS, Syndrome X, non- autoimmune Alzheimer's Disease, and autoimmune disease. One of skill in the art would not read the art of record to teach these uses. For example, one

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of skill in the art would read BABISH *et al.*, U.S. '098 and U.S. '350, to teach the use of "andrographolide" as a diterpene triepoxide lactone or triptolide adjunct. Similarly, one of skill in the art would read BOGGS *et al.*, U.S. '269 to teach the use of "andrographolide" as an antibiotic adjunct.

5 11. I respectfully disagree with the Examiner's factual assertion that "bacterial infection is broadly encompassed by AIDS" because AIDS does not encompass bacterial infection. AIDS is caused by an infection by a retrovirus, not a bacterium. The two different classes of infection require two completely different therapies. For example, AIDS is treated by anti-retroviral drugs, while bacterial infection is treated by antibiotics. Further, anti-retroviral drugs are structurally dissimilar from antibiotics. Further, no anti-viral drug has been shown effective against bacterial infection, and no antibiotic has been shown effective against AIDS.

10 12. One of skill in the art would read NANDURI *et al.*, U.S. '196, to teach that "andrographolide"-containing preparations "have been assayed for the ability to decrease the expression and phosphorylation of p34^{cdc2} kinase, cyclin B and c-Moss for treating or preventing pathogenicity." One of skill in the art would read NANDURI '196, however, to fail to teach *the results* of those assays (that is, he fails to say whether or not the assays show any effect). One of skill in

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the art would read NANDURI '196 to therefore provide a mere "invitation to experiment," not an enabling prior art disclosure of the claimed uses.

13. One of skill in the art would read PANOSIAN *et al.*, to teach the use of "andrographolide" for "in vitro effect on the activation and proliferation of immunocompetent cells." In contrast, autoimmune disease is thought to be caused by an overly-active immune system. Therefore, by teaching that andrographolide *activates* the immune system, one of skill in the art would read PANOSIAN to teach away from the use of the claimed compound to treat autoimmune diseases.

14. One of skill in the art would read WHEELOCK *et al.*, WO '213 to teach oncology and tumor treatment. One of skill in the art would read WHEELOCK *et al.*, U.S. '994, to teach anal tumor treatment.

15. One of skill in the art would understand that predictability in the pharmaceutical art is low because minor structural differences can precipitate major changes in toxicology or clinical efficacy. This shows that it would not have been obvious to modify any of the prior art compounds to *make* the claimed compound, and that it would not have been obvious to *use* such a modified compound for the claimed uses.

Juan Luis HANCKE OROZCO *et al.*
Serial No. 10/516,500
Priority Date: 03 February 2004
Diterpene Labdanes . . .

I further hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both,
5 under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

10 Professor Juan Luis HANCKE OROZCO, Ph.D.
Dated as of 9 September 2006

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DECLARATION - Page 9

Juan Luis HANCKE OROZCO *et al.*
Serial No. 10/316,500
Priority Date: 03 February 2004
Diterpenic Lanthanes...

I further hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both,

5 under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

10 
Professor Juan Luis HANCKE OROZCO, Ph.D.
Dated as of 9 September 2006

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